AMENDMENTS TO THE SPECIFICATION

PLEASE AMEND THE PARAGRAPH STARTING ON PAGE 8, LINE 16, AS FOLLOWS:

In an embodiment of this invention, the compounds of general formula I according to ~~claims~~ aspects 8 to 11 are used as preferred compounds. In this case, these are known compounds that are described in WO 97/267017. Their production can also be found in this WO publication. Surprisingly enough, it has been shown that these compounds are also very well suited as MRI-contrast media for visualization of thrombi. As quite especially preferred compounds, metal complexes MK 2, 3 and 4, as well as MK 8, 9, 10 and 11 (cf. also Table 1) are used.

Aspect is 8 is the use according to the invention, wherein as perfluoroalkyl-containing metal complexes, the compounds of general formula I are used

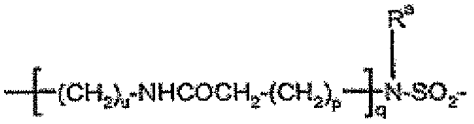
$$R^F\text{-}L\text{-}K \qquad I$$

in which

R^F is a perfluorinated, straight-chain or branched carbon chain with formula $-C_nF_{2n}E$, in which

E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom and n stands for numbers 4-30,

L means a direct bond, a methylene group, an -NHCO group, a group



whereby p means the numbers 0 to 10, and q and u, independently of one

another, mean numbers 0 or 1, and

R^a is a hydrogen atom, a methyl group, a benzyl group, a phenyl group, a $-CH_2-OH$ group, a CH_2OCH_3 group, a $-CH_2-CO_2H$ group or a C_2-C_{15} chain, which optionally is interrupted by 1 to 3 oxygen atoms, 1 to 2 >CO groups or an optionally substituted aryl group and/or is substituted with 1 to 4 hydroxyl groups, 1 to 2 C_1-C_4 alkoxy groups, 1 to 2 carboxy groups, or a group $-SO_3H$-,

or is a straight-chain, branched, saturated or unsaturated C_2-C_{30} carbon chain, which optionally contains 1 to 10 oxygen atoms, 1 to 3 $-NR^a$ groups, 1 to 2 sulfur atoms, a piperazine, a $-CONR^a$ group, one to six $-NR^aCO$ groups, an $-SO_2$ group, an $-NR^a-CO_2$ group, 1 to 2 CO groups, a group

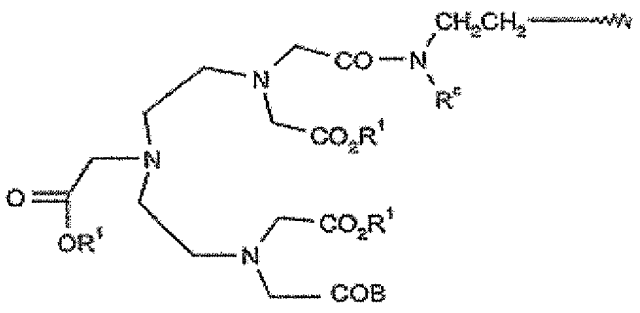
, or 1 to 2 optionally substituted aryls and/or is interrupted by these groups and/or is optionally substituted with 1 to 3 $-OR^a$ groups, 1 to 2 oxo groups, 1 to 2 $-NH-COR^a$ groups, 1 to 2 $-CONHR^a$ groups, 1 to 2 $-(CH_2)_p-CO_2H$ groups, 1 to 2 groups $-(CH_2)_p-(O)_q-CH_2CH_2-R^F$,

whereby

R^a, R^F and p and q have the above-indicated meanings, and

T means a C_2-C_{10} chain, which optionally is interrupted by 1 to 2 oxygen atoms or 1 to 2 -NHCO groups,

K stands for a complexing agent or metal complex or their salts of organic and/or inorganic bases or amino acids or amino acid amides, specifically for a complexing agent or complex of general formula II



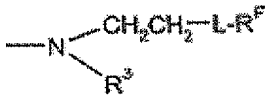
(II)

in which R^c, R^1 and B are independent of one another, and

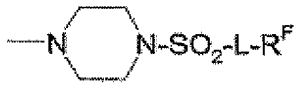
R^c has the meaning of R^a or means $-(CH_2)m-L-R^F$, whereby m is 0, 1 or 2, and L and R^F have the above-mentioned meaning,

R^1, independently of one another, mean a hydrogen atom or a metal ion equivalent of atomic numbers 22-29, 42-46 or 58-70,

B means $-OR^1$ or

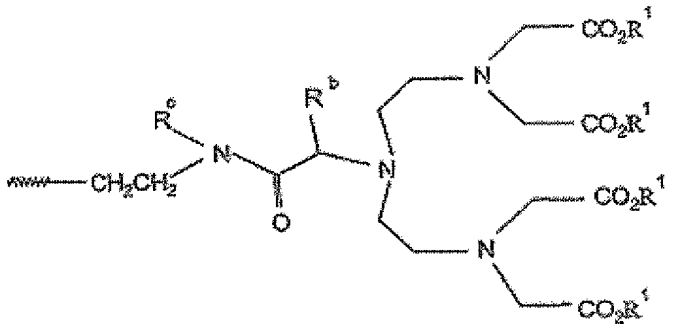


or



whereby R^1, L, R^F and R^c have the above-mentioned meanings, or

K stands for a complexing agent or complex of general formula III



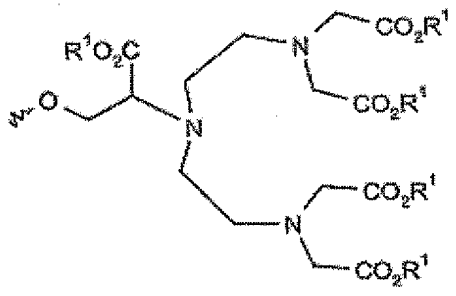
(III)

in which R^c and R^1 have the above-mentioned meanings,

R^b has the meaning of R^a,

or

K stands for a complexing agent or complex of general formula IV

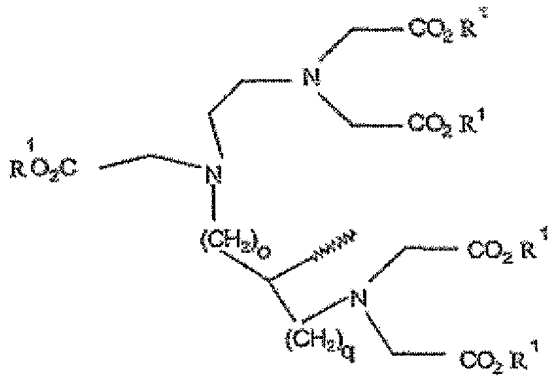


(IV)

in which R^1 has the above-mentioned meaning

or

K stands for a complexing agent or complex of general formula V

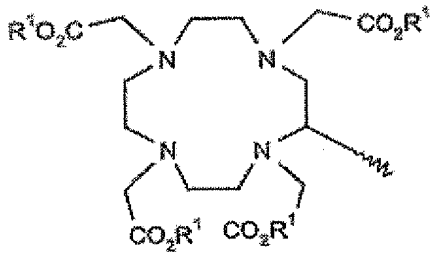


(V)

in which R^1 has the above-mentioned meaning, and o and q stand for number 0 or 1, and yields the sum o + q = 1,

or

K stands for a complexing agent or complex of general formula VI

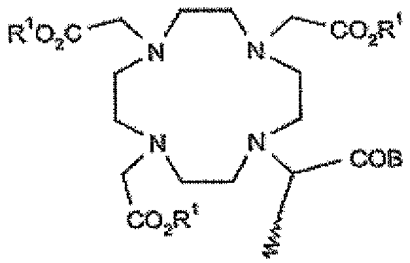


(VI)

in which R^1 has the above-mentioned meaning

or

K stands for a complexing agent or complex of general formula VII

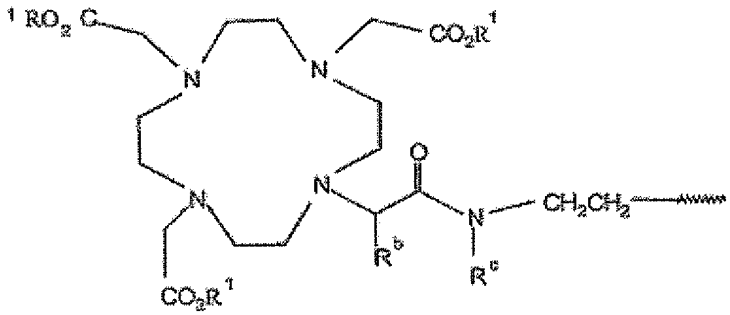


(VII)

in which R^1 and B have the above-mentioned meanings

or

K stands for a complexing agent or complex of general formula VIII

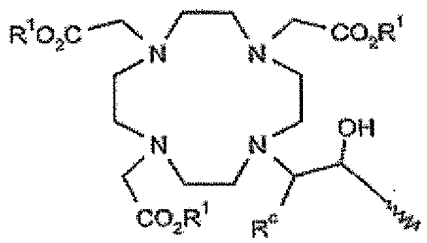


(VIII)

in which R^c and R^1 have the above-mentioned meanings, and R^b has the above-mentioned meaning of R^a

or

K stands for a complexing agent or complex of general formula IX

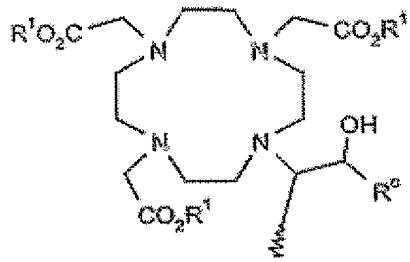


(IX)

in which R^c and R^1 have the above-mentioned meanings,

or

K stands for a complexing agent or complex of general formula X

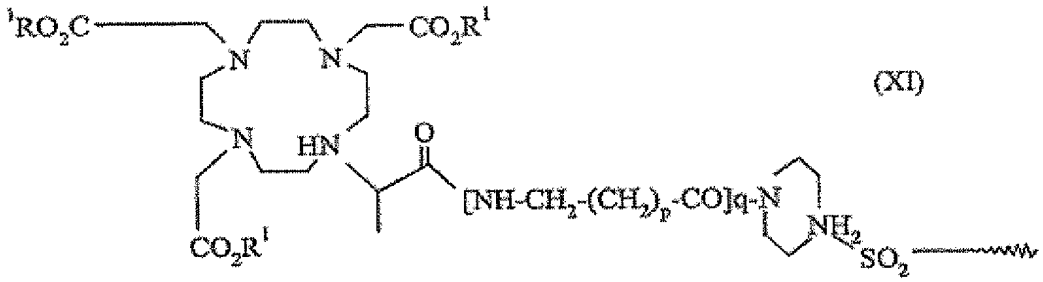


(X)

in which R^c and R^1 have the above-mentioned meanings,

or

K stands for a complexing agent or complex of general formula XI

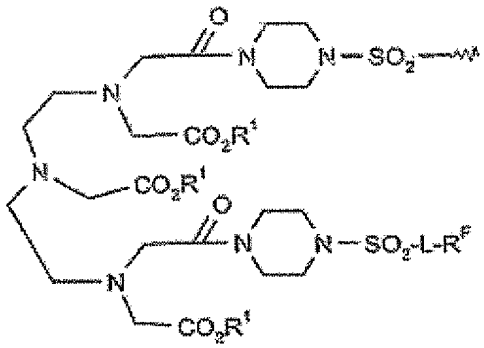


(XI)

in which R^1, p and q have the above-mentioned meaning, and R^b has the meaning of R^a,

or

K stands for a complexing agent or complex of general formula XII

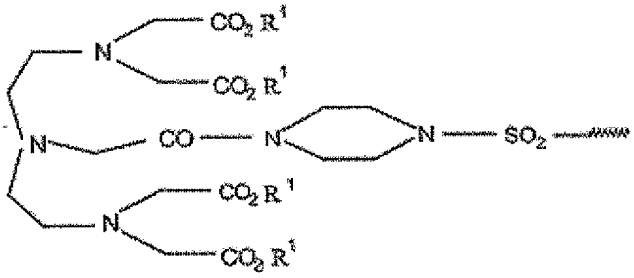


(XII)

in which L, R^F and Z^1 have the above-mentioned meanings,

or

K stands for a complexing agent or complex of general formula XIII



(XIII)

in which R^1 has the above-mentioned meaning,

are used.

Aspect 9 is the use according to aspect 8, wherein the compounds of general formula I, in which L stands for

α-CH_2-β
α-CH_2CH_2-β
α-$(CH_2)_s$-β s = 3 - 15
α-CH_2-O-CH_2CH_2-β
α-CH_2-(O-CH_2-CH_2-)$_t$-β t = 2 - 6
α-CH_2-NH-CO-β
α-CH_2-NH-CO-CH_2-N(CH_2COOH)-SO_2-β

α-CH_2-NH-CO-CH_2-N(C_2H_5)-SO_2-β

α-CH_2-NH-CO-CH_2-N($C_{10}H_{21}$)-SO_2-β

α-CH_2-NH-CO-CH_2-N(C_6H_{13})-SO_2-β

α-CH_2-NH-CO-$(CH_2)_{10}$-N(C_2H_5)-SO_2-β

α-CH_2-NH-CO-CH_2-N(-CH_2-C_6H_5)-SO_2-β

α-CH_2-NH-CO-CH_2-N(-CH_2-CH_2-OH)SO_2-β

α-CH_2-NHCO-$(CH_2)_{10}$-S-CH_2CH_2-β

α-CH_2NHCOCH_2-O-CH_2CH_2-β

α-CH_2NHCO$(CH_2)_{10}$-O-CH_2CH_2-β

α-CH_2-C_6H_4-O-CH_2CH_2-β

α-CH_2-O-CH_2-C(CH_2-OCH_2CH_2-C_6F_{13})$_2$-CH_2-OCH_2-CH_2-β

α-CH_2-NHCOCH_2CH_2CON-CH_2CH_2NHCOCH_2N(C_2H_5)$SO_2C_8F_{17}$

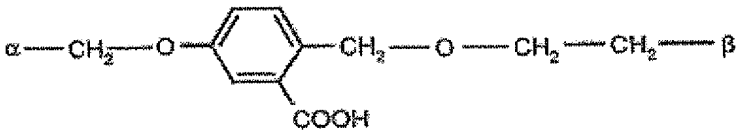
CH_2-CH_2NHCOCH_2N(C_2H_5)-SO_2-β

α-CH_2-O-CH_2-CH($OC_{10}H_{21}$)-CH_2-O-CH_2CH_2-β

α-(CH_2NHCO)$_4$-CH_2O-CH_2CH_2-β

α-(CH_2NHCO)$_3$-CH_2O-CH_2CH_2-β

α-CH_2-OCH_2C(CH_2OH)$_2$-CH_2-O-CH_2CH_2-β



α-CH_2NHCOCH_2N(C_6H_5)-SO_2-β

α-NHCO-CH_2-CH_2-β

α-NHCO-CH_2-O-CH_2CH_2-β

α-NH-CO-β

α-NH-CO-CH_2-N(CH_2COOH)-SO_2-β

α-NH-CO-CH_2-N(C_2H_5)-SO_2-β

α-NH-CO-CH_2-N($C_{10}H_{21}$)-SO_2-β

α-NH-CO-CH_2-N(C_6H_{13})-SO_2-β

α-NH-CO-$(CH_2)_{10}$-N(C_2H_5)-SO_2-β

α-NH-CO-CH_2-N(-CH_2-C_6H_5)-SO_2-β

α-NH-CO-CH_2-N(-CH_2-CH_2-OH)SO_2-β

α-NH-CO-CH_2-β

α-CH_2-O-C_6H_4-O-CH_2-CH_2-β
α-CH_2-C_6H_4-O-CH_2-CH_2-β
α-N(C_2H_5)-SO_2-β
α-N(C_6H_5)-SO_2-β
α-N($C_{10}H_{21}$)-SO_2-β
α-N(C_6H_{13})-SO_2-β
α-N(C_2H_4OH)-SO_2-β
α-N(CH_2COOH)-SO_2-β
α-N($CH_2C_6H_5$)-SO_2-β
α-N-[$CH(CH_2OH)_2$]-SO_2-β
α-N-[$CH(CH_2OH)CH(CH_2OH)$]-SO_2-β

and in which α represents the binding site to the complexing agent or metal complex K, and β represents the binding site to the fluorine radical,

are used.

Aspect 10 is the use according to aspects 8 and/or 9, wherein the compounds of formula I in which n in formula -$C_nF_{2n}E$ stands for numbers 4-15 and/or E in this formula means a fluorine atom are used.

Aspect 11 is the use according to one of aspects 8 to 10, wherein the following compounds are used:

-- Gadolinium complex of 10-[1-methyl-2-oxo-3-aza-5-oxo-{4-perfluorooctylsulfonyl-piperazin-1-yl}-pentyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,

-- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-oxa-10,10,11,11,12,12,13,13,14,14,15,15,16,16,17,17-heptadecafluoroheptadecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,

-- Gadolinium complex of 10-[2-hydroxy-4-aza-5,9-dioxo-9-{4-perfluorooctyl)-piperazin-1-yl}-nonyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,

-- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-aza-7-(perfluorooctyl-sulfonyl)-nonyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,

-- Gadolinium complex of 10-[2-hydroxy-4-oxa-1H,1H,2H,3H,3H,5H,5H,6H,6H-perfluorotetradecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,

-- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-oxa-10,10,11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,19,19-henicosafluoro-nonadecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,

-- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-11-aza-11-(perfluorooctylsulfonyl)-tridecyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane,

-- Gadolinium complex of 10-[2-hydroxy-4-aza-5-oxo-7-aza-7-(perfluorooctylsulfonyl)-8-phenyl-octyl]-1-4-7-tris(carboxymethyl)-1,4,7,10-tetraaza-cyclododecane.

PLEASE AMEND THE PARAGRAPH STARTING ON PAGE 8, LINE 22, AS FOLLOWS:

In another embodiment of this invention, those compounds of general formula Ia according to ~~claims~~ aspects 12 to 21 are used as preferred compounds. These compounds are known and are described in WO 99/01161. Their use as MRI contrast media for visualization of thrombi still had not been described to date. Of these compounds, quite especially preferably metal complex MK 12 (cf. Table 1) is used.

Aspect 12 is the use according to the invention, wherein as perfluoroalkyl-containing metal complexes, the compounds of general formula Ia are used

$$A\text{-}R^F \qquad \text{(Ia)}$$

in which

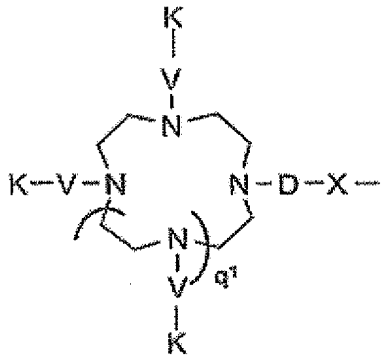
- A is a molecule part that contains 2 to 6 metal complexes, which are bonded directly or via a linker to a nitrogen atom of an annular skeleton chain, and

- R^F is a perfluorinated, straight-chain or branched carbon chain with formula $-C_nF_{2n}E$, in which

  E represents a terminal fluorine, chlorine, bromine, iodine or hydrogen atom,

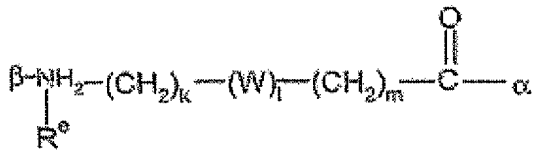
  and n stands for numbers 4-30,

whereby molecule part A has the following structure:

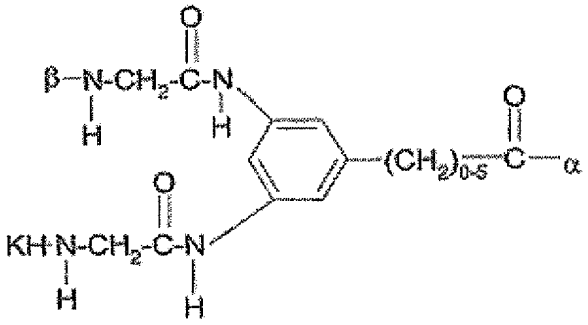


whereby

- q^1 is a number 0, 1, 2 or 3,
- K stands for a complexing agent or metal complex or their salts of organic and/or inorganic bases or amino acids or amino acid amides,
- X is a direct bond to the perfluoroalkyl group, a phenylene group or a C_1-C_{10}-alkylene chain, which optionally contains 1-15 oxygen atoms, 1-5 sulfur atoms, 1-10 carbonyl groups, 1-10 (NR^d) groups, 1-2 NR^dSO_2 groups, 1-10 $CONR^d$ groups, 1 piperidine group, 1-3 SO_2 groups and 1-2 phenylene groups or optionally is substituted by 1-3 radicals R^F, in which R^d stands for a hydrogen atom, a phenyl group, benzyl group or a C_1-C_{15} alkyl group, which optionally contains 1-2 NHCO groups, 1-2 CO groups, or 1-5 oxygen atoms and optionally is substituted by 1-5 hydroxy, 1-5 methoxy, 1-3 carboxy, or 1-3 R^F radicals,
- V is a direct bond or a chain of general formula IIa or IIIa:



(IIa)



(IIIa)

in which

- R^e is a hydrogen atom, a phenyl group, a benzyl group or a C_1-C_7-alkyl group, which optionally is substituted with a carboxy group, a methoxy group or a hydroxy group,
- W is a direct bond, a polyglycol ether group with up to 5 glycol units, or a molecule part of general formula IVa

$$-CH(R^h)- \qquad \text{(IVa)}$$

in which R^h is a C_1-C_7 carboxylic acid, a phenyl group, a benzyl group or a $-(CH_2)_{1-5}$-NH-K group,

- α represents the binding to the nitrogen atom of the skeleton chain, β represents the binding to complexing agents or metal complex K,
- and in which variables k and m stand for natural numbers between 0 and 10, and l stands for 0 or 1

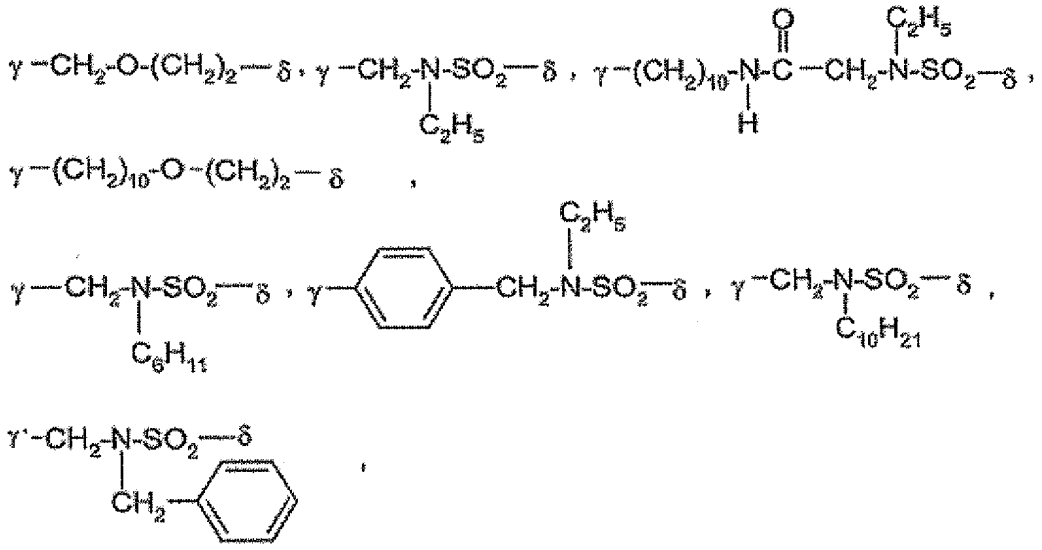
and whereby

- D is a CO or SO_2 group,

are used.

Aspect 13 is the use according to aspect 12, wherein the compounds of general formula Ia in which q is the number 1 are used.

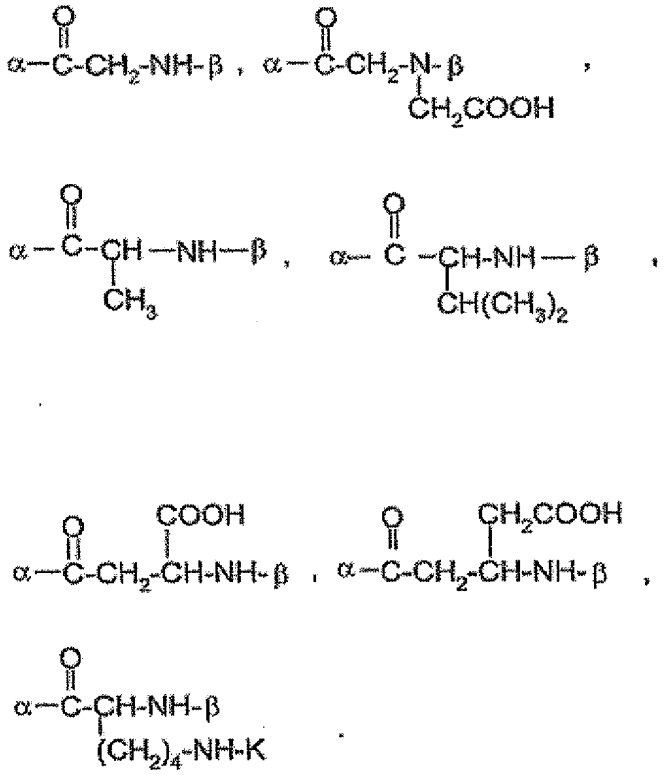
Aspect 14 is the use according to aspect 12, wherein the compounds of general formula Ia are used, in which molecule part X is an alkylene chain, which contains 1-10 CH_2CH_2O groups or 1-5 $COCH_2NH$ groups, a direct bond or one of the following structures



whereby

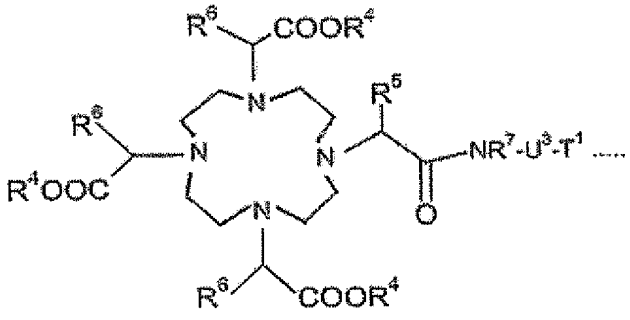
γ binds to D, and δ binds to R^F.

Aspect 15 is the use according to aspect 12, wherein the compounds of general formula Ia, in which V is a molecule part with one of the following structures

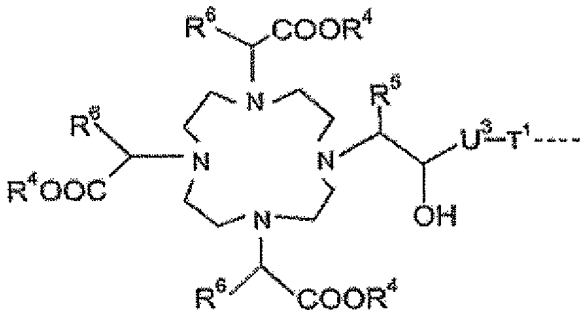


are used.

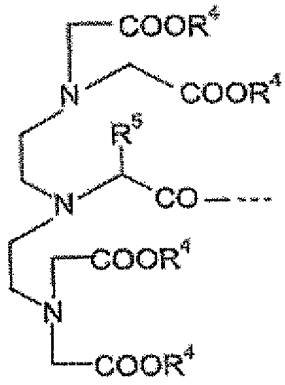
Aspect 16 is the use according to aspect 12, wherein the compounds of general formula Ia, in which K represents a complex of general formula Va, VIa, VIIa or VIIIa,



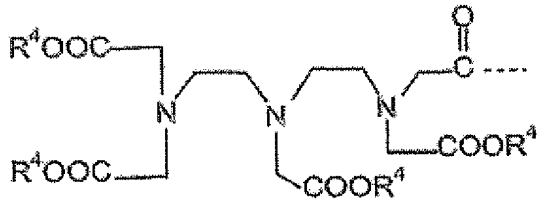
(Va)



(VIa)



(VIIa)



(VIIIa)

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are used,

whereby

- R^4, independently of one another, are a hydrogen atom or a metal ion equivalent

of the elements of atomic numbers 23-29, 42-46 or 58-70,

- R^5 is a hydrogen atom or a straight-chain, branched, saturated or unsaturated C_1-C_{30} alkyl chain, which optionally is substituted by 1-5 hydroxy, 1-3 carboxy or 1 phenyl group(s) and/or optionally is interrupted by 1-10 oxygen atoms, 1 phenylene group or 1 phenylenoxy group,
- R^6 is a hydrogen atom, a straight-chain or branched C_1-C_7 alkyl radical, a phenyl radical or a benzyl radical,
- R^7 is a hydrogen atom, a methyl group or ethyl group, which optionally is substituted by a hydroxy group or carboxy group,
- U^3 is a straight-chain, branched, saturated or unsaturated C_1-C_{20} alkylene group optionally containing 1-5 imino groups, 1-3 phenylene groups, 1-3 phenylenoxy groups, 1-3 phenylenimino groups, 1-5 amide groups, 1-2 hydrazide groups, 1-5 carbonyl groups, 1-5 ethylenoxy groups, 1 urea group, 1 thiourea group, 1-2 carboxyalkylimino groups, 1-2 ester groups, 1-1-0 oxygen atoms, 1-5 sulfur atoms and/or 1-5 nitrogen atoms, and/or optionally substituted by 1-5 hydroxy groups, 1-2 mercapto groups, 1-5 oxo groups, 1-5 thioxo groups, 1-3 carboxy groups, 1-5 carboxyalkyl groups, 1-5 ester groups and/or 1-3 amino groups, whereby the optionally contained phenylene groups can be substituted by 1-2 carboxy groups, 1-2 sulfone groups or 1-2 hydroxy groups
- T^1 stands for a -CO-β, -NHCO-β or -NHCS-β group, whereby β represents the binding site to V.

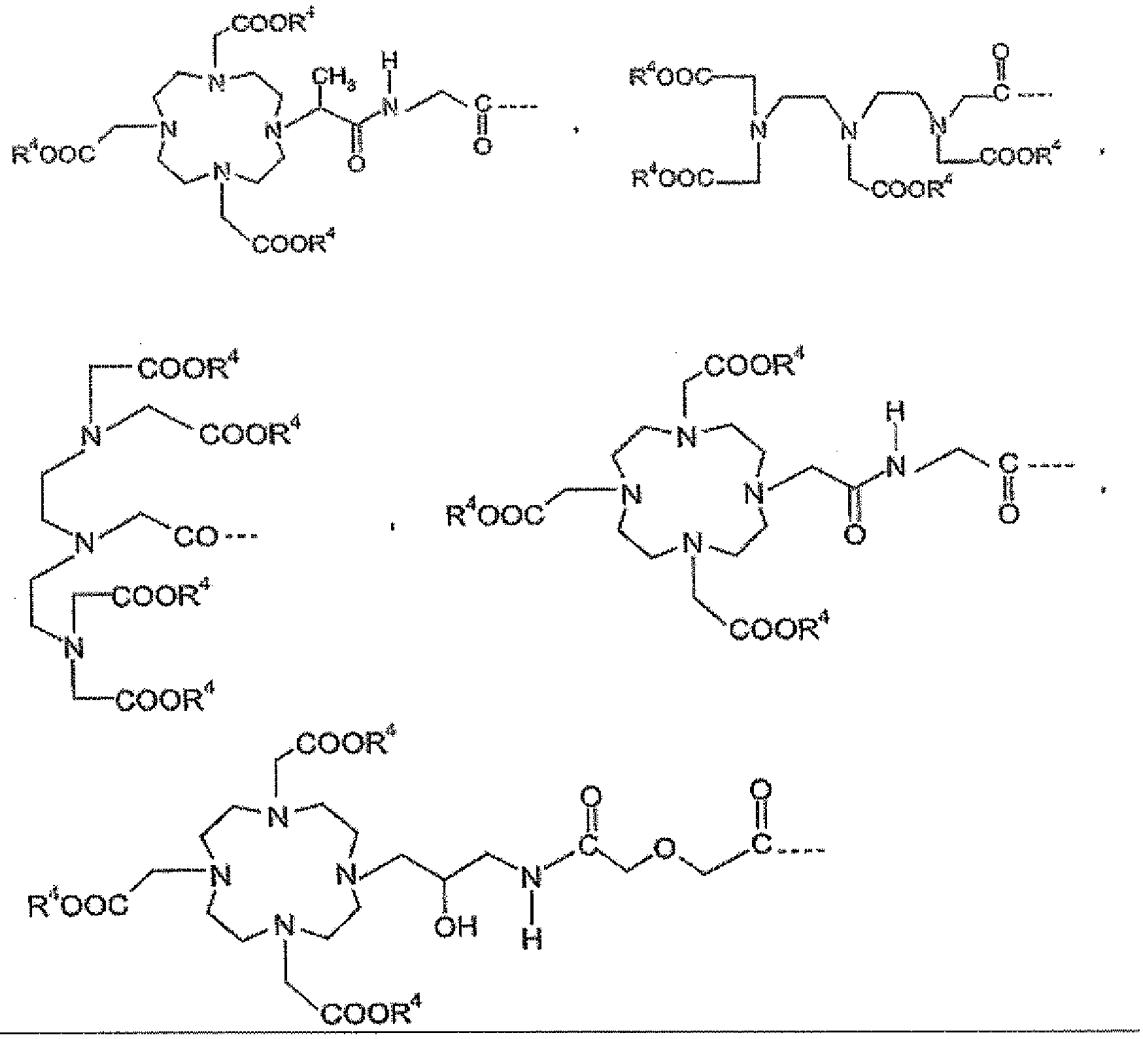
Aspect 17 is the use according to aspect 16, wherein the C_1-C_{20}-alkylene chain that stands for U^3 contains the groups -CH_2NHCO-, -$NHCOCH_2O$-, -$NHCOCH_2OC_6H_4$-, -$N(CH_2CO_2H)$-, -CH_2OCH_2-, -$NHCOCH_2C_6H_4$-, -$NHCSNHC_6H_4$-, -$CH_2OC_6H_4$-, -CH_2CH_2O- and/or is substituted by the groups -COOH and -CH_2COOH.

Aspect 18 is the use according to aspect 16, wherein U^3 stands for a -CH_2-, -CH_2CH_2-, -$CH_2CH_2CH_2$-, -C_6H_4-, -C_6H_{10}-, -$CH_2C_6H_4$-, -$CH_2NHCOCH_2CH(CH_2CO_2H)$-$C_6H_4$-, -

$CH_2NHCOCH_2OCH_2$-, or

$-CH_2NHCOCH_2C_6H_4$- group.

Aspect 19 is the use according to aspect 12, wherein the compounds of general formula Ia in which K has one of the following structures:



are used.

Aspect 20 is the use according to one of aspects 12 to 19, wherein the compounds of general formula Ia in which the perfluoroalkyl chain R^F is $-C_6F_{13}$, $-C_8F_{17}$, $-C_{10}F_{21}$ or $-C_{12}F_{25}$ are used.

Aspect 21 is the use according to one of aspects 12 to 20, wherein the gadolinium complex of 1,4,7-tris{1,4,7-tris(N-(carboxylatomethyl)-10-[N-1-methyl-3,6-diaza-2,5,8-trioxooctane-1,8-diyl)]-1,4,7,10-tetraazacyclododecane, Gd complex}-10-[N-2H,2H,4H,4H,5H,5H-3-oxa-perfluorotridecanoyl]-1,4,7,10-tetraazacyclododecane is used.